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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/046,649	01/14/2002	Richard A. Young	2869.1001-023	3487

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/046,649	YOUNG ET AL.	
	Examiner	Art Unit	
	Stacy B Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10/14/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's amendment filed October 9, 2003 is acknowledged and entered. Claims 43-75 are pending and examined. All previous rejections under 35 U.S.C. 112 and 35 U.S.C. 102(b) are moot in view of Applicant's cancellation of claim 13.

Priority

2. This application claims priority back to USSN 07/207,298 filed June 15, 1988, now abandoned. Upon review of the disclosures of the applications relating to the instant application, it has been determined that the disclosure of the application USSN 08/073,381, filed June 4, 1993, is the earliest filed application that supports the subject matter of claims 43-75. The application USSN 07/804,632 filed December 9, 1991, does not disclose hsp-antigen complexes. Therefore, the claimed subject matter is entitled to the priority of the filing date of the application USSN 08/073,381, filed June 4, 1993.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 43-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cox *et al.* (*Eur. J. Immunol.*, 1988, 18:2015-2019), previously made of record, in view of Thole *et al.* (*Infection and Immunity*, 1987, 55:1466-1475) and Traversari *et al.* (*J. Exp. Med.*, 1992,

176:1453-1457). The claims are drawn to a composition comprising a stress protein, or portion thereof, and a melanoma antigen peptide, wherein the composition, when administered to an individual, induces or enhances an immune response against the melanoma antigen peptide. The stress protein can be the *M. bovis* BCG hsp65 protein, which is fused via a peptide bond or chemically conjugated to the melanoma antigen. Also claimed is a composition consisting of a stress protein, or portion thereof, and a melanoma antigen peptide, wherein the composition, when administered to an individual, induces or enhances an immune response against the melanoma antigen peptide. Pharmaceutical compositions of the stress protein-melanoma antigen compositions are claimed which have a pharmaceutically acceptable carrier or excipient. Also claimed are isolated nucleic acids encoding the protein of the composition.

Cox teaches a fusion protein comprising part of a stress protein, linked by a peptide bond to a viral peptide, administration of the fusion protein to an animal and an improved immune response induced by the fusion (abstract). The stress protein is derived from a T cell epitope in the 65-kDa protein of *M. tuberculosis* or the 65 kDa protein of *M. leprae*. These proteins have been sequenced. The stress proteins were synthesized with an added cysteine residue on the carboxy terminus to facilitate coupling and to enhance immunogenicity (page 2015, Materials and Methods). The bond between the cysteines is a disulfide bond, which is a peptide bond, and also is within the definition of a chemical conjugate. Cox does not teach a *M. bovis* BCG hsp65 protein, or a melanoma antigen.

However, Thole discloses a 64-65 kDa protein of *M. bovis* BCG and sequence encoding the protein that is involved in eliciting cellular immunity to mycobacterial infections (page 1466, first and second column, bridging paragraph, and page 1473, second column). Traversari

discloses a nonapeptide encoded by human gene MAGE-1 that is recognized by cytotoxic T cells (abstract).

It would have been obvious to substitute the protein of Thole and the antigen of Traversari into the fusion protein of Cox. One would have been motivated to substitute *M. bovis* BCG hsp65 protein for 65-kDa protein of *M. tuberculosis* or the 65 kDa protein of *M. leprae* because these proteins are similar in structure (65-kDa) and function (eliciting a cellular response). Cox's reasoning for choosing the 65-kDa protein of *M. tuberculosis* and the 65 kDa protein of *M. leprae* is that they are T-cell epitopes. Thole shows that the *M. bovis* BCG hsp65 protein is involved in eliciting a T-cell response. One would have had a reasonable expectation of success that the *M. bovis* BCG hsp65 protein would have worked in the fusion protein of Cox because the proteins of Cox and the protein of Thole are involved in a T-cell response.

It would have been obvious to substitute the melanoma antigen of Traversari into the Cox fusion protein. Cox's fusion protein comprises a stress protein and a viral antigen. One would have been motivated to substitute Traversari's melanoma antigen into Cox's fusion protein because Cox suggests combining heterologous peptides with stress proteins for potential peptide vaccines (page 2015). One would have had a reasonable expectation of success that the melanoma antigen would have worked in the fusion protein of Cox, because the melanoma antigen, when administered, is known to treat melanoma patients (page 303, first column). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 43-75 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10, 14-28, 32-47, 51-59, 70-74, 85-89 of U.S. Patent No. 6,338,952 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the application are, in some instances, an obvious species of the patented genus. For example, claims of the patent are drawn to a fusion protein comprising a stress protein and a cancer antigen. The instant claims are drawn to a composition comprising a stress protein fused to a melanoma antigen. The melanoma antigen would have been an obvious species of patented genus, cancer antigen, because the melanoma antigen was known at the time of the invention (Traversari *et al.* (*J. Exp. Med.*, 1992, 176:1453-1457), and is disclosed in the 6,338,952 patent as a cancer antigen. In other instances, the patented claims are a species of the genus instantly claimed. Instant claim 43 is drawn to a composition comprising a stress protein and a melanoma antigen. The claims of the patent are drawn to a fusion protein comprising stress protein and heterologous antigen wherein they are bound by a peptide bond. In yet other instances, while the conflicting claims are not identical, they are obvious variants of each other. For example, the claims of application are drawn to a composition comprising a stress protein and a melanoma antigen. The claims of the patent are drawn to an isolated fusion protein comprising a stress protein and a cancer antigen. It would have been obvious to incorporate the fusion protein into a composition because the patented claims are not only drawn to an isolated fusion protein, but to a composition comprising the fusion protein. The isolated fusion proteins, the compositions comprising the fusion proteins, the compositions consisting of the fusion proteins, the pharmaceutical composition comprising

fusion proteins, the pharmaceutical compositions comprising compositions comprising fusion proteins, etc., are all obvious variants of each other.

Conclusion

5. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers relating to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 located in Crystal Mall 1. The Fax number for Art Unit 1648 is (703) 872-9306. All Group 1600 Fax machines will be available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Stacy B. Chen, whose telephone number is (571) 272-0896. The Examiner can normally be reached on Monday through Friday from 7:30 AM-4:00 PM, (EST). If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, James C. Housel, can be reached at (571) 272-0902. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SBC
Stacy B. Chen
January 22, 2004

James C. Housel 1/24/04
JAMES HOUSEL
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